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=> D HIS

     (FILE 'HOME' ENTERED AT 19:14:39 ON 06 SEP 91)

     FILE 'REGISTRY' ENTERED AT 19:15:02 ON 06 SEP 91
L1             1 S 82186-77-4/RN
L2             1 S 75887-54-6/RN
L3             1 S 71963-77-4
L4             1 S 63968-64-9/RN
L5             1 S 88495-63-0/RN

=> FILE CA
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       5.86       6.11

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diagrams.


=> S L1
L6             4 L1

=> S L2 OR L3 OR L4 OR L5
              24 L2
              57 L3
             206 L4
              40 L5
L7           274 L2 OR L3 OR L4 OR L5

=> S MALARIA? OR ANTIMALARIA? OR ANTI-MALARIA?
            2264 MALARIA?
            2298 ANTIMALARIA?
           22560 ANTI
            2264 MALARIA?
              16 ANTI-MALARIA?
                 (ANTI(W)MALARIA?)
L8          3821 MALARIA? OR ANTIMALARIA? OR ANTI-MALARIA?

=> S L6 AND L7
L9             0 L6 AND L7

=> S L6 AND L8
L10            3 L6 AND L8

=> S L7 AND L8
L11           95 L7 AND L8

=> D L10 1-3 BIB AB

L10  ANSWER 1 OF 3
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AN   CA114(1):6046p
TI   Improved synthesis of antimalarial fluorenemethanol derivative
AU   Deng, Rongxian; Zhong, Jingxing; et al.
```

CS Chinese Academy of Military Medical Sciences, Microbiology and Epidemic Disease Institute
LO Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp.
PI CN 1042535 A 30 May 1990
AI CN 88-107666 10 Nov 1988
IC ICM C07C215-88
ICS C07C025-22; C07C049-807
SC 25-26 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
SX 1
DT P
CO CNXXEV
PY 1990
LA Ch
AB Fluorenemethanol deriv. (I), an antimalarial 3.2 times more effective than chloroquine, is prepd. by an improved method which avoids the use of environmentally harmful diazomethane and dichloramine T. Reductive cyclization of chloroacetyl deriv. II (R = ClCH2CO) (prepn. given) with KBH4 in EtOH gave 70-80% epoxide deriv. II (R = oxiranyl), which was refluxed with Bu2NH in EtOH to give 80-85% amino alc. deriv. II [R = CH(OH)CH2NBu2] (III). Condensation of III with p-ClC6H4CHO in the presence of granular NaOH in EtOH gave 60-70% I.

L10 ANSWER 2 OF 3

AN CA101(16):136941u
TI Stability of antimalarial fluorenemethanol in soft capsules
AU Wang, Yunling; Ding, Jianxin; Geng, Rongliang
CS Inst. Microbiol. Epidemiol., Mil. Acad. Med. Sci.
LO Beijing, Peop. Rep. China
SO Yaowu Fenxi Zazhi, 4(2), 84-7
SC 63-5 (Pharmaceuticals)
DT J
CO YFZADL
IS 0254-1793
PY 1984
LA Ch
AB The stability of fluorenemethanol (I) [82186-77-4] soft capsules contg. linoleic acid was studied. TLC indicated that an impurity tentatively identified as I linoleate [92069-16-4] was obsd. The empirical formula was C48H62O2NCl3 an the solidifying point was -52 to -53.degree.. The mol. wt. detd. by mass spectrometry was identical to the theor. value. I and I linoleate were detd. by spectrophotometry at 335 nm. The std. curve was linear to .apprx.40 .mu.g and recoveries were 98.33 and 99.97%, resp. The formation of I linoleate increased with temp. from 60 to 120.degree..

L10 ANSWER 3 OF 3

AN CA97(4):28538h
TI Enhancement of bioavailability of a hydrophobic fluorenemethanol antimalarial by oleic acid in soft gelatin capsules
AU Wang, Yunling; Ding, Deben; Ding, Jianxin
CS Microb. Epidemics Inst., Acad. Mil. Med.
LO Peop. Rep. China
SO Yaoxue Tongbao, 17(1), 4-7
SC 63-6 (Pharmaceuticals)
DT J
CO YHTPAD
IS 0512-7343
PY 1982
LA Ch
AB Antimalarial .alpha.-(dibutylaminomethyl)-.alpha.-[2,7-dichloro-9-(4-

chlorobenzylidene)-4-fluorenyl]methanol (I) [82186-77-4] was highly sol. in oleic acid [112-80-1] or linoleic acid [60-33-3] (>350 mg I/mL), but the soly. of I in water was extremely low (.apprx.1 .mu.g I/mL). An aq. soln. of I was barely absorbable. Thus, I soft gelatin capsules with high absorbability were prepd. contg. I 3.5 g, vitamin E (antioxidant) 2 mg, Tween 80 (surfactant) 0.k g and oleic acid or linoleic acid to 10 g.

=> D L11 5-10 BIB AB

L11 ANSWER 5 OF 95

AN CA114(2):12187b
TI Method for the isolation of artemisinin from Artemisia annua
AU Elferaly, Farouk S.; Elsohly, Hala N.
LO USA
SO U.S., 4 pp.
PI US 4952603 A 28 Aug 1990
AI US 88-208763 20 Jun 1988
IC ICM A61K031-335
NCL 514450000
SC 63-4 (Pharmaceuticals)
DT P
CO USXXAM
PY 1990
LA Eng
AB An improved method of producing artemisinin (I), an antimalarial agent, from the leaves of Artemisia annua comprises (1) extg. the plant with hexane, (2) partitioning the hexane ext. between hexane and MeCN-H2O mixt., (3) evapg. the MeCN phase to dryness, (4) chromatographing the evapd. mixt. on silica gel adsorbent with a solvent comprising EtOAc in hexane, and (5) evapg. the solvent followed by crystn. to produce substantially pure I. This invention provides a simple, practical method for the isolation and recovery of I from plant material which yields I in quantities and purity unobtainable in the methods known in the prior art. Also, this process allows the eluting columns to be used in .gtoreq.2 runs, resulting in economic advantages.

L11 ANSWER 6 OF 95

AN CA114(1):6866f
TI Acid degradation products of qinghaosu and their structure-activity relationships
AU Imakura, Yasuhiro; Hachiya, Katsutoshi; Ikemoto, Tomomi; Yamashita, Shinsuke; Kihara, Masaru; Kobayashi, Shigeru; Shingu, Tetsuro; Milhous, Wilbur K.; Lee, Kuo Hsiung
CS Fac. Sci., Naruto Univ. Educ.
LO Naruto 772, Japan
SO Heterocycles, 31(6), 1011-16
SC 30-15 (Terpenes and Terpenoids)
SX 1
DT J
CO HTCYAM
IS 0385-5414
PY 1990
LA Eng
AB Treatment of qinghaosu (I) with acid yielded 1',2',4'-trioxanes II (R = Me, Et) endoperoxides III, and diketones IV. Structures II-IV were assigned based on their phys. and spectral data. Structure-activity correlation among these compds. indicated the steric requirement of the 1',2',4'-trioxane ring system as found in I was required for potent antimalarial activity.

L11 ANSWER 7 OF 95
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AN CA114(1):127u
TI Structure elucidation and thermospray high-performance liquid chromatography/mass spectroscopy (HPLC/MS) of the microbial and mammalian metabolites of the antimalarial arteether
AU Hufford, Charles D.; Lee, Ik Soo; ElSohly, Hala N.; Chi, Hsien Tao; Baker, John K.
CS Sch. Pharm., Univ. Mississippi
LO University, MS 38677, USA
SO Pharm. Res., 7(9), 923-7
SC 1-2 (Pharmacology)
SX 10
DT J
CO PHREEB
IS 0724-8741
PY 1990
LA Eng
AB Microbial metab. studies of the antimalarial drug arteether (I) have shown that I is metabolized to 6 new metabolites in addn. to those previously reported. Large-scale fermns. with Cunninghamella elegans (ATCC 9245) and Streptomyces lavendulae (L-105) have resulted in the characterization of these metabolites primarily by two-dimensional NMR (2D-NMR) methods as 9.beta.-hydroxyI, a ring rearrangement metabolite, 3.alpha.-hydroxy-11-epideoxydihydroartemisinin, 9.alpha.-hydroxyI, 2.alpha.-hydroxyI, and 14-hydroxyI. Thermospray mass spectroscopy/high-performance liq. chromatog. analyses have shown that 4 of these metabolites are also present in rat liver microsome prepns.

L11 ANSWER 8 OF 95
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AN CA113(11):97856w
TI Deoxoartemisinin: new compound and composition for the treatment of malaria
AU McChesney, James D.; Jung, Mankil
LO USA
SO U.S., 3 pp.
PI US 4920147 A 24 Apr 1990
AI US 89-329669 28 Mar 1989
IC ICM A61K031-335
ICS C07D321-02
NCL 514450000
SC 30-15 (Terpenes and Terpenoids)
SX 1
DT P
CO USXXAM
PY 1990
LA Eng
AB The title compd. (I) was prepd. Thus, artemisinin and BF3.Et2O in THF were added to an ice-cooled soln of NaBH4 in THF. The mixt was stirred 1 h at ice temp and refluxed 10 min to give I. I had an IC50 of 0.15 ng/mL against Plasmodium falciparum UV-2.

L11 ANSWER 9 OF 95
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AN CA113(5):41044n
TI A short and stereospecific synthesis of (+)-deoxoartemisinin and (-)-deoxodesoxyartemisinin
AU Jung, Mankil; Li, Xun; Bustos, Daniel A.; ElSohly, Hala N.; McChesney, James D.
CS Sch. Pharm., Univ. Mississippi
LO University, MS 38677, USA

FILE COPY

D L1 FCN STR *

L1 ANSWER 1 OF 1
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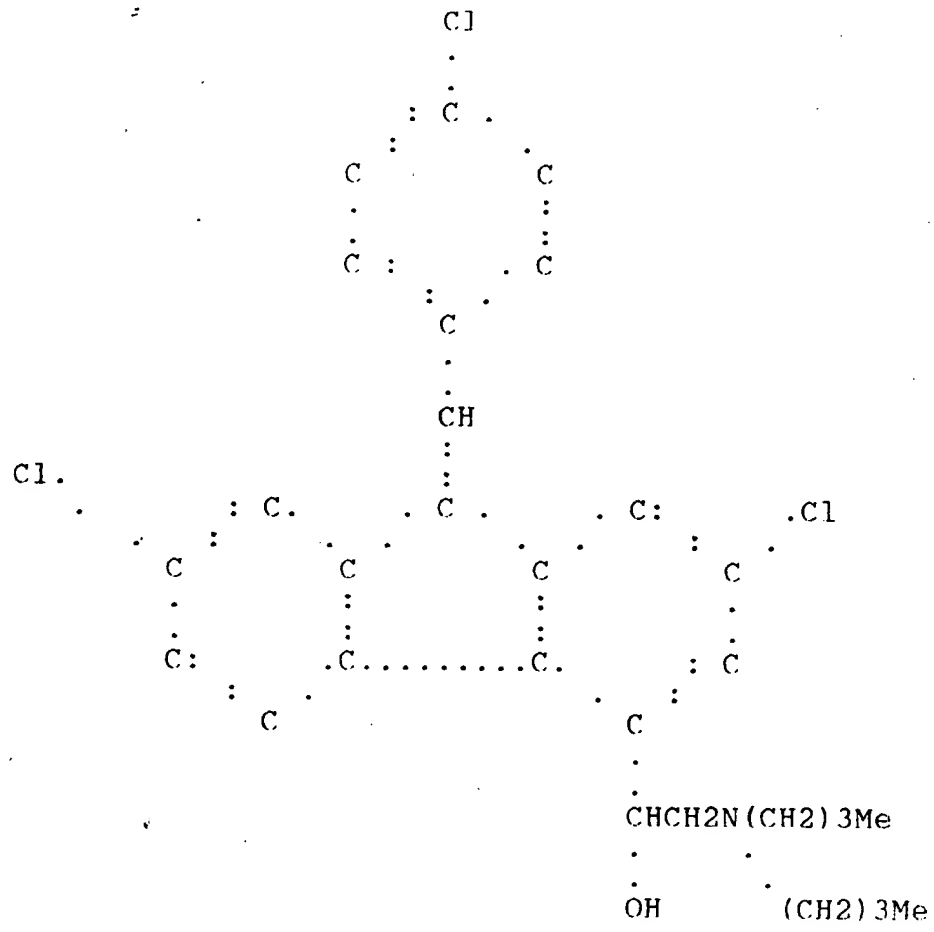
CN 9H-Fluorene-4-methanol, 2,7-dichloro-9-[(4-chlorophenyl)methylene]-.alpha.-[(dibutylamino)methyl]- (9CI) (CA INDEX NAME)
CN Benflumelol



=> S 75887-54-6/RN
L2 1 75887-54-6/RN

=> D L2 FNC STR
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For an explanation, enter 'HELP DISPLAY'.

=> D L2 FCN STR

L2 ANSWER 1 OF 1
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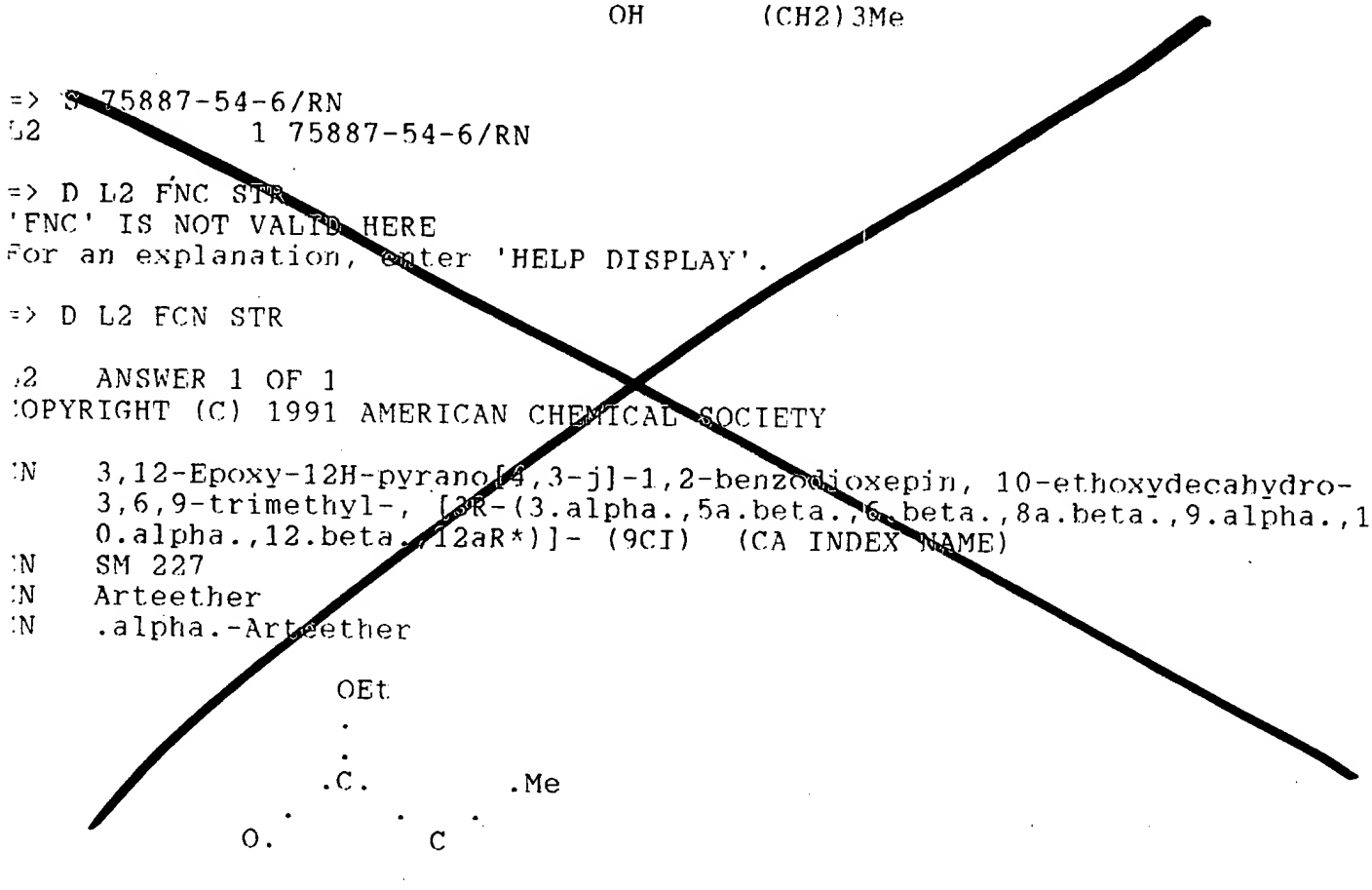
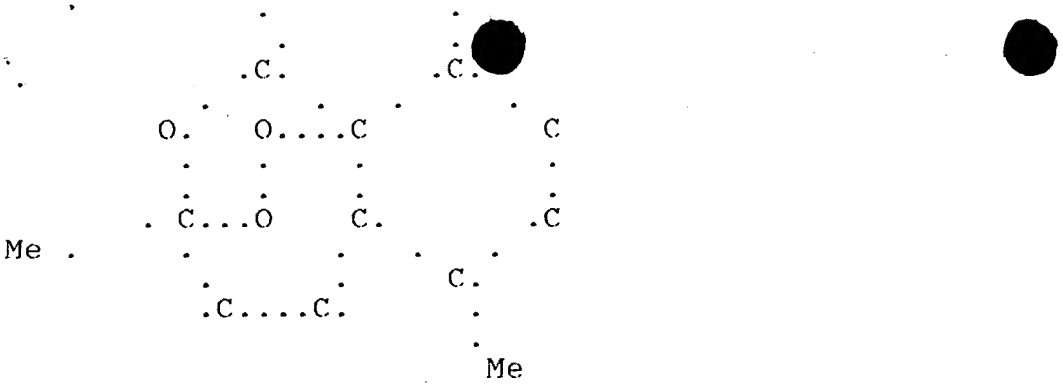
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-ethoxydecahydro-3,6,9-trimethyl-, [3R-(3.alpha.,5a.beta.,6.beta.,8a.beta.,9.alpha.,10.alpha.,12.beta.,12aR*)]- (9CI) (CA INDEX NAME)
CN SM 227
CN Arteether
CN .alpha.-Arteether



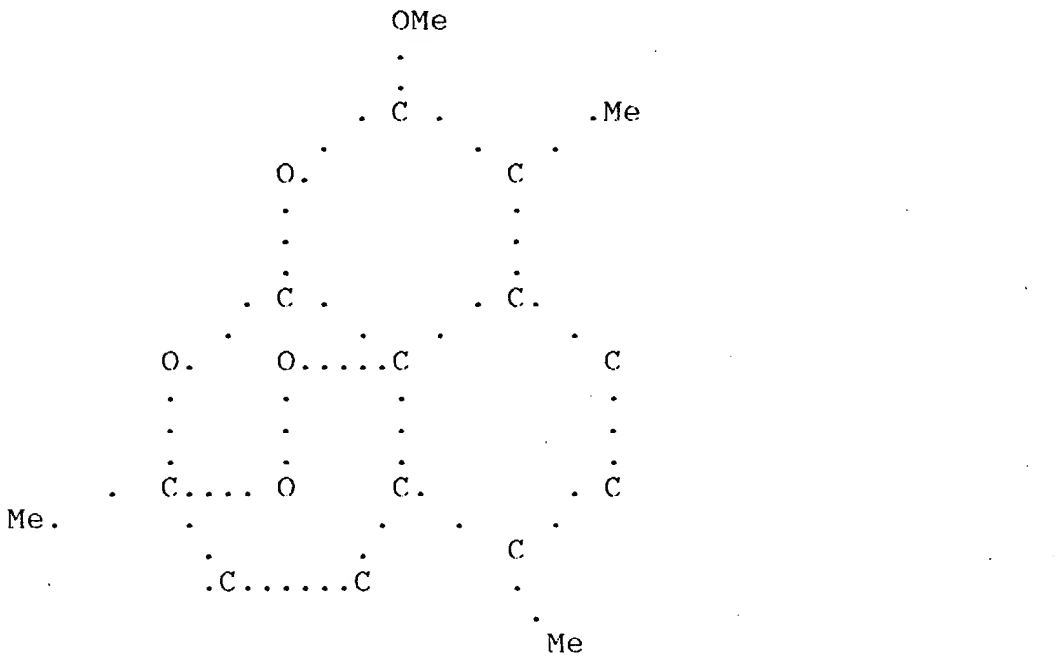


=> S 71963-77-4
L3 1 71963-77-4
(71963-77-4/RN)

=> D L3 FCN STR

L3 ANSWER 1 OF 1

CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, decahydro-10-methoxy-3,6,9-trimethyl-, [3R-(3.alpha.,5a.beta.,6.beta.,8a.beta.,9.alpha.,10.alpha.,12.beta.,12aR*)]- (9CI) (CA INDEX NAME)
CN Artemether
CN SM 224
CN Dihydroartemisin methyl ether



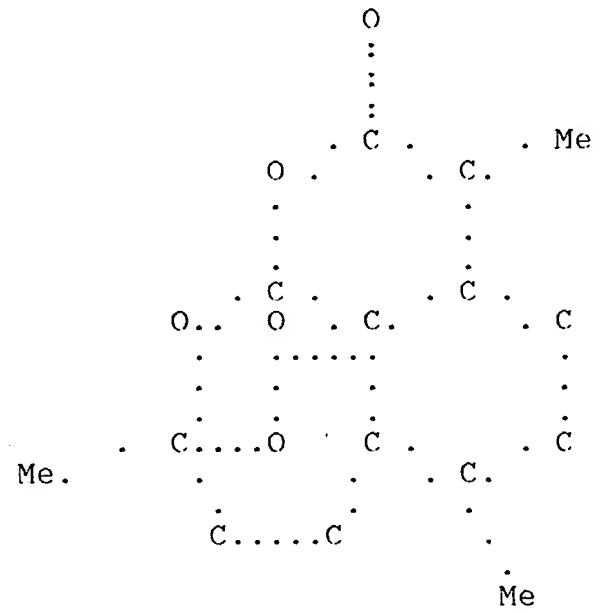
=> S 63968-64-9/RN
L4 1 63968-64-9/RN

=> D L4 FCN STR

L4 ANSWER 1 OF 1

CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10(3H)-one, octahydro-3,6,9-trimethyl-, [3R-(3.alpha.,5a.beta.,6.beta.,8a.beta.,9.alpha.,12.beta.,12aR*)]- (9CI) (CA INDEX NAME)
CN Qing Hau Sau

CN Artemisinin
CN Arteannuin
CN Qinghaosu
CN Qing Hau Su
CN (+)-Artemisinin
CN Qinghosu
CN (+)-Arteannuin

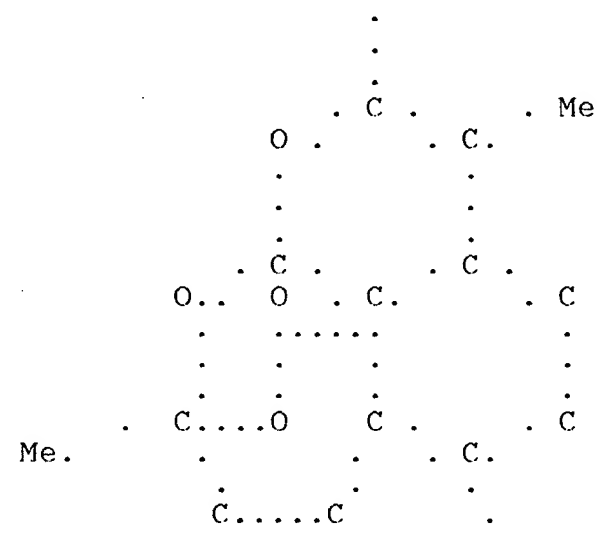


=> S 88495-63-0/RN
L5   1 88495-63-0/RN

=> D L5 FCN STR

L5 ANSWER 1 OF 1

CN Butanedioic acid, mono(decahydro-3,6,9-trimethyl-3,12-epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin-10-yl) ester, [3R-(3.alpha.,5a.beta.,6.beta.,8a.beta.,9.alpha.,10.alpha.,12.beta.,12aR*)]- (9CI) (CA INDEX NAME)
CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, butanedioic acid deriv. (9CI)
CN Artesunic acid
CN Artesunate
CN Qinghaozhi



SO Tetrahedron Lett., 30(44), 5973-6
SC 30-15 (Terpenes and [redacted]rpenoids)
DT J
CO TELEAY
IS 0040-4039
PY 1989
LA Eng
OS CASREACT 113:41044
AB The synthesis of (+)-deoxoartemisinin (I; Z = H, H) and (-)-deoxodesoxyartemisinin (II) was achieved either from artemisinic acid (III) or from artemisinin (I; Z = 0).

L11 ANSWER 10 OF 95 ✱

AN CA113(5):34389a
TI Systemic toxicity study of a new schizontocidal antimalarial drug, Arteether, in rats and monkeys
AU Sethi, N.; Srivastava, S.; Murthy, P. S. R.; Singh, R. K.
CS Div. Toxicol., Cent. Drug Res. Inst.
LO Lucknow 226001, India
SO Indian J. Parasitol., 12(2), 223-35
SC 1-5 (Pharmacology)
DT J
CO IJPAES
IS 0253-7168
PY 1988
LA Eng
AB Six wk toxicity testing of a newly prepd. antimalarial drug, Arteether (I), was carried out in rats and monkeys. The routine toxicity parameters in hematol., biochem., and histopathol. of the animals did not reveal any significant change as compared to the control. It has been concluded from the expts. that compd. is safe in rodents and nonhuman primates at the doses used.

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	18.73	24.84

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.06	-3.06

STN INTERNATIONAL LOGOFF AT 19:23:27 ON 06 SEP 91

US PAT NO: 4,816,478 L7: 5 of 6
DATE ISSUED: Mar. 28, 1989
TITLE: Treatment of acquired immunodeficiency syndrome
INVENTOR: Carl R. Thornfeldt, 1054 N.W. 2nd Ave., Ontario, OR 97914
APPL-NO: 07/088,437
DATE FILED: Aug. 24, 1987
ART-UNIT: 125
PRIM-EXMR: Jerome D. Goldberg
LEGAL-REP: Townsend and Townsend

4,816,478 1 CLASSIFICATIONS L7: 5 of 6

1. 514/450 OR

US PAT NO: 4,816,478 L7: 5 of 6

ABSTRACT:
A treatment of Acquired Immunodeficiency Syndrome (AIDS) and AIDS Related Complex (ARC) with therapeutically effective amounts of semisynthetic derivatives of dihydroartemesinin and synthetic compounds with a sesquiterpene structure.

US PAT NO: 4,791,135 L7: 6 of 6
DATE ISSUED: Dec. 13, 1988
TITLE: Novel antimalarial dihydroartemisinin derivatives
INVENTOR: Ai J. Lin, Gaithersburg, MD
Daniel L. Klayman, Chevy Chase, MD
Wilbur K. Milhous, Rockville, MD
ASSIGNEE: The United States of America as represented by the Secretary of the Army, Washington, DC (U.S. govt.)
APPL-NO: 07/087,365
DATE FILED: Aug. 20, 1987
ART-UNIT: 121
PRIM-EXMR: Jane T. Fan
LEGAL-REP: Anthony T. Lane, William V. Adams, Werten F. W. Bellamy

4,791,135 2 CLASSIFICATIONS L7: 6 of 6

1. 514/450 OR
2. 549/348 XR

US PAT NO: 4,791,135 L7: 6 of 6

ABSTRACT:
This invention relates to novel dihydroartemisinin derivatives, including their pharmaceutically-acceptable salts, which are therapeutically-effective in the pre- and post-treatment of malarial infections.

=>

ABSTRACT:
A process for synthesizing oxygen-containing polyoxatetracycle compounds and in particular analogs of the antimalarial agent known as qinghaosu or artemisinin is disclosed. The process employs as a reactant an olefinically unsaturated bicyclic bridging ketone having nonenolizable bridgehead moieties for both of its alpha positions. This ketone is converted to a vinylsilane that is subjected to ozonolytic cleavage of its olefinic bond to yield a member of a family of unique carboxyl/carbonyl-substituted vinylsilanes which may in turn optionally be subjected to a wide range of reactions prior to a final ozonolysis/acidification step which closes the oxygen-containing ring structure. The various intermediates are claimed as aspects of this invention as are novel tetracycles and their use as antimalarials .

US PAT NO: 5,011,951 [IMAGE AVAILABLE] L7: 3 of 6
DATE ISSUED: Apr. 30, 1991
TITLE: Synthesis of artemisininelactol derivatives
INVENTOR: Peter Buchs, Bioggio, Switzerland
Arnold Brossi, Bethesda, MD
ASSIGNEE: World Health Organization, Switzerland, Switzerland (foreign corp.)
APPL-NO: 07/316,282
DATE FILED: Feb. 27, 1989
ART-UNIT: 126
PRIM-EXMR: Nicky Chan

5,011,951 [IMAGE AVAILABLE] 1 CLASSIFICATIONS L7: 3 of 6

1. 549/348 OR

US PAT NO: 5,011,951 [IMAGE AVAILABLE] L7: 3 of 6

ABSTRACT:
A process for the epimerization of .alpha.- to .beta.-ethyletherartemisininelactol (arteether) or preparation of arteether , useful in the treatment of malaria, from artemisininelactol, comprises reacting starting material in a solvent including an acid catalyst, the reaction of artemisininelactol also including an etherifying ethyl moiety, and isolating the product.

US PAT NO: 4,978,676 [IMAGE AVAILABLE] L7: 4 of 6
DATE ISSUED: Dec. 18, 1990
TITLE: Treatment of skin diseases with artemisinin and derivatives
INVENTOR: Carl R. Thornfeldt, 1054 NW. 2nd Ave., Ontario, OR 97914
APPL-NO: 07/335,615
DATE FILED: Apr. 10, 1989
ART-UNIT: 125
PRIM-EXMR: Leonard Schenkman
LEGAL-REP: Townsend and Townsend

4,978,676 [IMAGE AVAILABLE] 2 CLASSIFICATIONS L7: 4 of 6

1. 514/450 OR
2. 514/863 XR

US PAT NO: 4,978,676 [IMAGE AVAILABLE] L7: 4 of 6

ABSTRACT:
Psoriasis, ultraviolet light induced skin conditions and tumors are successfully treated with topical or oral administration of artemisinin, dihydroartemisinin, its [redacted]isynthetic derivatives an[redacted]its synthetic analogs. Viral tumors/diseases, hemorrhoids, and bullous skin diseases are also successfully treated with these topical compositions.

d 17 1-6 bib cls ab

US PAT NO: 5,021,426 [IMAGE AVAILABLE] L7: 1 of 6
DATE ISSUED: Jun. 4, 1991
TITLE: Method of traeting malaria with cyproheptadine derivatives
INVENTOR: John J. Baldwin, Gwynedd Valley, PA
Gabriel F. Eilon, Irvine, CA
Paul A. Friedman, Rosemont, PA
David C. Remy, North Wales, PA
ASSIGNEE: Merck & Co., Inc., Rahway, NJ (U.S. corp.)
APPL-NO: 07/484,774
DATE FILED: Feb. 26, 1990
ART-UNIT: 129
PRIM-EXMR: Glennon H. Hollrah
ASST-EXMR: Gary E. Hollinden
LEGAL-REP: Hesna J. Pfeiffer, Raymond M. Speer, William H. Nicholson

5,021,426 [IMAGE AVAILABLE] 5 CLASSIFICATIONS L7: 1 of 6

1. 514/313 OR
2. 514/314 XR
3. 514/318 XR
4. 514/325 XR
5. 514/895 XR

US PAT NO: 5,021,426 [IMAGE AVAILABLE] L7: 1 of 6

ABSTRACT:
Various 3-substituted cyproheptadine derivatives are useful in the treatment of infection by Plasmodium falciparum and in the treatment of malaria either as compounds, pharmaceutically acceptable salts, or pharmaceutical composition ingredients in combination with antimalarial agents or compounds. Methods of treating malaria and methods of treating infection by Plasmodium falciparum are also described.

US PAT NO: 5,019,590 [IMAGE AVAILABLE] L7: 2 of 6
DATE ISSUED: May 28, 1991
TITLE: Antimalarial analogs of artemisinin
INVENTOR: Mitchell A. Avery, Palo Alto, CA
Wesley K. M. Chong, Mountain View, CA
ASSIGNEE: SRI International, Menlo Park, CA (U.S. corp.)
APPL-NO: 07/414,730
DATE FILED: Sep. 27, 1989
ART-UNIT: 123
PRIM-EXMR: Jane T. Fan
LEGAL-REP: Richard P. Lange

5,019,590 [IMAGE AVAILABLE] 9 CLASSIFICATIONS L7: 2 of 6

1. 514/450 OR
2. 514/453 XR
3. 549/276 XR
4. 549/277 XR
5. 549/279 XR
6. 549/348 XR
7. 556/436 XR
8. 556/489 XR
9. 568/374 XR

US PAT NO: 5,019,590 [IMAGE AVAILABLE] L7: 2 of 6

D L1 FCN STR

L1 ANSWER 1 OF 1
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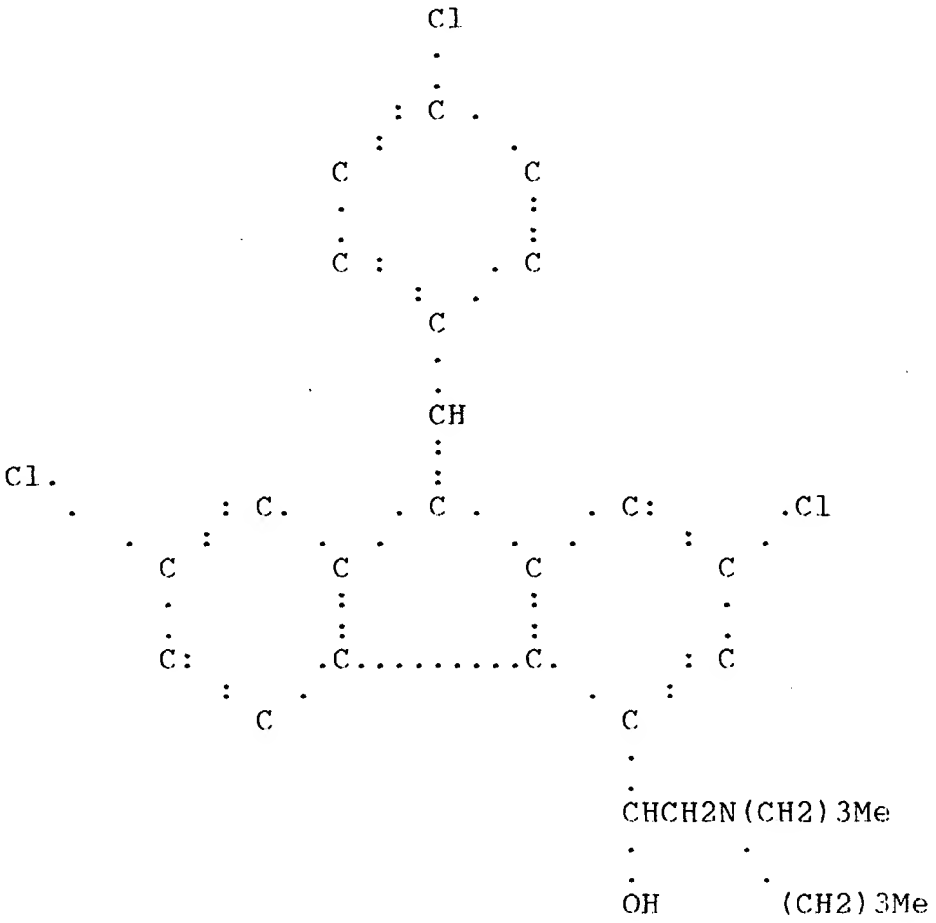
CN 9H-Fluorene-4-methanol, 2,7-dichloro-9-[(4-chlorophenyl)methylene]-
.alpha.-[(dibutylamino)methyl]- (9CI) (CA INDEX NAME)
CN Benflumelol



=> S 75887-54-6/RN
L2 1 75887-54-6/RN

=> D L2 FNC STR
'FNC' IS NOT VALID HERE
For an explanation, enter 'HELP DISPLAY'.

=> D L2 FCN STR

L2 ANSWER 1 OF 1
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CN 3,12-Epoxy-12H-pyrano[4,3-j]-1,2-benzodioxepin, 10-ethoxydecahydro-
3,6,9-trimethyl-, [3R-(3.alpha.,5a.beta.,6.beta.,8a.beta.,9.alpha.,1
0.alpha.,12.beta.,12aR*)]- (9CI) (CA INDEX NAME)
CN SM 227
CN Arteether
CN .alpha.-Arteether